UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/524,815	02/18/2005	Erich Gulbins	AERX-134	1995

24353 7590 12/18/2009

BOZICEVIC, FIELD & FRANCIS LLP
1900 UNIVERSITY AVENUE
SUITE 200
EAST PALO ALTO, CA 94303

EXAMINER	
JEAN-LOUIS, SAMIRA JM	

ART UNIT	PAPER NUMBER
1627	

MAIL DATE	DELIVERY MODE
12/18/2009	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/524,815	GULBINS, ERICH	
	Examiner	Art Unit	
	SAMIRA JEAN-LOUIS	1627	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *04 December 2009*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☐ Claim(s) *40 and 42-46* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *40 and 42-46* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Response to Arguments

This Office Action is in response to the amendment submitted on 12/04/09. Claims 40 and 42-46 are currently pending in the application, with claims 1-39 and 41 having being cancelled. Accordingly, claims 40 and 42-46 are being examined on the merits herein.

Receipt of the aforementioned amended claims and Certified English Translation of the original German application is acknowledged and has been entered.

Applicant's argument with respect to the rejection of claims 40, 42, 44, and 46 under 35 U.S.C. § 103(a) has been fully considered. Given that applicant has perfected priority under 35 U.S.C. 119 (a)-(d), Grassme is no longer qualified as prior art. Consequently, the rejection of claims 40, 42, 44, and 46 under 35 U.S.C. § 103(a) is hereby withdrawn.

Applicant's argument with respect to the rejection of claims 43 and 45 under 35 U.S.C. § 103(a) has been fully considered. Given that applicant has perfected priority under 35 U.S.C. 119 (a)-(d), Grassme is no longer qualified as prior art or as a primary reference. Consequently, the rejection of claims 43 and 45 under 35 U.S.C. § 103(a) over Grassme in view of Albouz and in further view of Daines and Bilgi is hereby withdrawn.

Applicant's argument with respect to the rejection of claim 43 under 35 U.S.C. § 103(a) has been fully considered. Given that applicant has amended the claims, such rejection is now moot. Consequently, the rejection of claim 43 under 35 U.S.C. § 103(a) is hereby withdrawn.

For the foregoing reasons, the rejections of record and the Finality of such rejections are hereby withdrawn. However, the following modified 103 (a) Final rejections are being made.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 40, 42, and 44-46 are rejected under 35 U.S.C. 103 (a) as being unpatentable over Ni et al. (U.S. 6,608,101 B1) in view of Chen et al. (U.S. 6,248,528, B1) and in further view of Daines (U.S. 5,569,677, previously cited).

Ni et al. teach 1,3-bis-(substituted-phenyl)-2-propen-1-ones for inhibiting expression of VCAM-1 and useful to treat a patient with a disorder mediated by V-CAM-1 including cystic fibrosis (see abstract, col. 10, lines 5-12, and col. 15, lines 6-9). In fact, Ni et al. teach that VCAM is upregulated in a wide variety of disease states including cystic fibrosis (see col. 43, lines 55-59). Additionally, Ni et al. teach that the compounds of the instant invention can be combined with a second biologically active agent to increase the effectiveness against the target disorder (see col. 44, lines 56-61). Specifically, Ni et al teach that the present invention can be combined with amitriptyline (instant claims 42, 44, and 45) or tricyclic-antidepressants (instant claim 42; see col. 47, lines 32-39 and col. 165, lines 37-38 and 59).

Ni et al. do not teach the use of imipramine as the tricyclic antidepressant in the treatment of cystic fibrosis.

Ni et al. however teach the use of secondary biologically active agents to help in the effectiveness of the disease being treated. Ni et al. further teach the use of amitriptyline and tricyclic anti-depressants as secondary biological active agents.

Chen et al. was provided to demonstrate that imipramine and amitriptyline are both tricyclic antidepressants (see col. 21, lines 39-40 and 49-50).
As a result, the Examiner maintains that one of ordinary skill in the art at the time of the invention was made would have found it obvious to substitute imipramine for the

amitriptyline of Ni et al. given that the substitution of one known element for another would have yielded predictable results.

Daines teaches pharmaceutical compositions containing leukotriene antagonists known to be useful in various diseases including cystic fibrosis (see abstract and col. 1, lines 40-45). Daines teaches that such compositions (i.e. pharmaceutical compositions designed for cystic fibrosis) can contain a pharmaceutically carrier or diluent depending upon the intended route of administration, for example parenterally, topically, orally, or by inhalation (instant claim 40; see col.7, lines 34-37, 52-55, and col. 11, example 3).

Thus, to one of ordinary skill in the art at the time of the invention would have found it obvious to utilize the combination of formula I and amitryptiline of Ni et al. for the treatment of cystic fibrosis since Ni et al. teach that such combination is effective in treating V-CAM associated disorders including cystic fibrosis. Similarly, one of ordinary skill in the art would have found it obvious to substitute imipramine for amitriptyline in the aforementioned combination since Chen demonstrated that both imipramine and amitriptyline are known equivalents and would thus be expected to behave similarly. Additionally, one of ordinary skill in the art at the time of the invention would have found it obvious to formulate the composition of Ni et al. as an inhalation composition since Daines teaches that compositions for the treatment of cystic fibrosis can be formulated in various forms including inhalation.

Moreover, it is well within the purview of the skilled artisan during routine experimentation to formulate the composition in various forms depending on desired ease of administration or desired rate of delivery of such composition. Thus, given the teachings of Ni, Chen and Daines, one of ordinary skill in the art would have been motivated to utilize amitryptiline or imipramine in the treatment of cystic fibrosis and further formulate it as an inhalable composition with the reasonable expectation of providing a method efficient in treating cystic fibrosis.

Claim 43 are rejected under 35 U.S.C. 103 (a) as being unpatentable over Ni et al. (U.S. 6,608,101 B1) in view of Chen et al. (U.S. 6,248,528, B1) and in further view of Daines (U.S. 5,569,677, previously cited) as applied to claims 40, 42 and 44-46 and in further view of Bilgi et al. (Canadian Family Physician. May 1979; Vol. 25, pgs. 619-620, 622, and 624-625, previously submitted).

The Ni, Chen and Daines references are as discussed above and incorporated by reference herein. However, Ni, Chen and Daines do not teach the antidepressant as a tetracyclic antidepressant.

Bilgi et al. teach that tricyclic antidepressants (TCA) are effective in treating depressive states but may impose minor therapeutic side effects (se pg. 619, left col.). Indeed, Bilgi et al. teach that treatment with tricyclic antidepressants such as amitriptyline, imipramine, and clomipramine caused various side effects including

hypotension, hypertension, arrhythmia, and sinus tachycardia (see pg. 620 and pg. 624, table 1). As for the tetracyclic antidepressant, maprotiline, Bilgi et al. teach that administration of maprotiline to healthy individuals resulted in minimal ST-T changes which later disappeared despite repeated administration of the compound (see pg. 622, right col., Paragraph 1 under maprotiline and its effects Section). In fact, Bilgi et al. teach that treatment with maprotiline can be given safely to cardiac patients as it improves ventricular function, end-diastolic pressure, and stroke work index and further suggest treatments with tetracyclic antidepressants to patients predisposed to cardiotoxicity to TCA (see pg. 622, right col., and pg. 625, Conclusion Section).

Thus, to one of ordinary skill in the art at the time of the invention would have found it obvious to utilize the tetracyclic amitryptiline of Bilgi et al. instead of the TCA of Ni et al. since Bilgi et al. teach them as equivalent TCA. Moreover, one of ordinary skill in the art would have found it obvious to utilize tetracyclic antidepressants as opposed to TCA since Bilgi et al. teach that tetracyclics pose minimal side effects and lead to improved ventricular function. Thus, given the teachings of Bilgi et al., one of ordinary skill in the art would have been motivated to substitute tetracyclics for the amitriptyline in the treatment of cystic fibrosis with the reasonable expectation of providing a method efficient in treating cystic fibrosis and a method that entails minimal side effects.

Conclusion

No claims are allowed.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Samira Jean-Louis whose telephone number is 571-270-3503. The examiner can normally be reached on 7:30-6 PM EST M-Th.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Sreeni Padmanabhan can be reached on 571-272-0629. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/S. J. L. /

Examiner, Art Unit 1627

12/15/2009

/SREENI PADMANABHAN/

Supervisory Patent Examiner, Art Unit 1627